

Bachelor Thesis

The first genome-scale reconstruction of *Corynebacterium simulans*

1 Background

Corynebacterium simulans is a Gram-positive and aerobic member of the phylum Actinobacteria. It was first described in 2000 as a non-lipophilic, fermentative species of the Genus *Corynebacterium* [11]. *C. simulans* is one of the less well-described *Corynebacteria*. Since the first report in 2000, there are not more than 30 reports in Pubmed journals on clinical microbiology and veterinary medicine journal combined. *C. simulans* and other Genus members are known as commensals of normal human flora, but they can occasionally act as pathogens. It was reported to inflict pyogenic spondylitis, a life-threatening condition [9]. Of note, *C. simulans* could be misclassified as *C. striatum* [7, 8]. Therefore, reconstructing the model can give more information about the qualitative attitude of this organism. It can also help in identifying the mechanisms which cause diseases or develop a therapy against them.

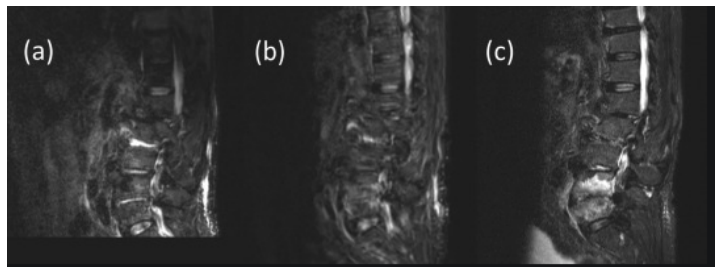


Figure 1 | Pyogenic spondylitis with acute course caused by *Corynebacterium simulans* [9].

2 Aim

This thesis aims to reconstruct and extend the model of *C. simulans* using automated tools such as CarveMe [6]. To build a precise and significant model and gain more information about the bacterium's role in the human body, manual curation by incorporating further information from relevant databases, such as KEGG [3], Bio-Cyc [4], is required [10]. Also, the mass and charge need to be balanced. Further mandatory additions to the model include annotations of metabolites, reactions, and genes, as well as Systems Biology Ontology (SBO) terms. QC/QA (quality control/quality assurance) techniques will be applied to validate the model. Since *C. simulans* occupies a habitat of the nasal bacterial community, the growth ability of the organism on the synthetic nasal medium (SNM3) [5], which mimics the human nose environment, will be examined. In the end, the interactions with other bacteria, most prominently with *Staphylococcus aureus*, will be simulated and analyzed theoretically.

3 Requirements

Experience in Python programming and familiarity with COBRApy [2] and libSBML [1] for the reconstruction process. High motivation to improve the model and gain more knowledge is also of vital importance.

References

- [1] Benjamin J. Bornstein, Sarah M. Keating, Akiya Jouraku, and Michael Hucka. LibSBML: an API library for SBML. *Bioinformatics*, 24(6):880–881, March 2008. doi:10.1093/bioinformatics/btn051.
- [2] Ali Ebrahim, Joshua A. Lerman, Bernhard ØPalsson, and Daniel R. Hyduke. COBRApy: CONstraints-Based Reconstruction and Analysis for Python. *BMC Systems Biology*, 7:74, August 2013. doi:10.1186/1752-0509-7-74. URL <http://www.biomedcentral.com/1752-0509/7/74>.
- [3] Minoru Kanehisa, Yoko Sato, Miho Furumichi, Kanae Morishima, and Mao Tanabe. New approach for understanding genome variations in KEGG. *Nucleic Acids Research*, 47(D1):D590–D595, January 2019. ISSN 13624962. doi:10.1093/nar/gky962.
- [4] Peter D. Karp, Richard Billington, Ron Caspi, Carol A. Fulcher, Mario Latendresse, Anamika Kothari, Ingrid M. Keseler, Markus Krummenacker, Peter E. Midford, Quang Ong, Wai Kit Ong, Suzanne M. Paley, and Pallavi Subhraveti. The BioCyc collection of microbial genomes and metabolic pathways. *Briefings in bioinformatics*, 20:1085–1093, July 2019. ISSN 1477-4054. doi:10.1093/bib/bbx085.
- [5] Bernhard Krismer, Christopher Weidenmaier, Alexander Zipperer, and Andreas Peschel. The commensal lifestyle of *Staphylococcus aureus* and its interactions with the nasal microbiota. *Nature reviews. Microbiology*, 15:675–687, October 2017. ISSN 1740-1534. doi:10.1038/nrmicro.2017.104.
- [6] Daniel Machado, Sergej Andrejev, Melanie Tramontano, and Kiran Raosaheb Patil. Fast automated reconstruction of genome-scale metabolic models for microbial species and communities. *Nucleic Acids Research*, 46(15):7542–7553, September 2018. ISSN 0305-1048. doi:10.1093/nar/gky537. URL <https://academic.oup.com/nar/article/46/15/7542/5042022>.
- [7] Allison R. McMullen, Neil Anderson, Meghan A. Wallace, Angela Shupe, and C. A. Burnham. When Good Bugs Go Bad: Epidemiology and Antimicrobial Resistance Profiles of *Corynebacterium striatum*, an Emerging Multidrug-Resistant, Opportunistic Pathogen. *Antimicrobial agents and chemotherapy*, 61, November 2017. ISSN 1098-6596. doi:10.1128/AAC.01111-17.
- [8] Rajeev Peeyush Nagassar, Alison Merle Nicholson, Winston Williams, and Roma Jaanki Bridgelal-Nagassar. Diphtheroids as a cause of endocarditis in a haemodialysis patient. *BMJ case reports*, 2012, May 2012. ISSN 1757-790X. doi:10.1136/bcr.2011.4894.
- [9] M. Ogasawara, T. Matsuhisa, T. Kondo, R. Oshima, F. Sugiura, T. Niwa, Y. Ando, M. Sato, J. Sato, and S. Kohri. Pyogenic spondylitis with acute course caused by *Corynebacterium simulans*. *Journal of Infection and Chemotherapy*, 26(3):294–297, March 2020. ISSN 1341-321X. doi:10.1016/j.jiac.2019.10.012. URL <https://doi.org/10.1016/j.jiac.2019.10.012>.
- [10] Ines Thiele and Bernhard Palsson. A protocol for generating a high-quality genome-scale metabolic reconstruction. *Nature Protocols*, 5(1):93–121, January 2010. ISSN 17542189. doi:10.1038/nprot.2009.203.
- [11] P. Wattiau, M. Janssens, and G. Wauters. *Corynebacterium simulans* sp. nov., a non-lipophilic, fermentative Corynebacterium. *International journal of systematic and evolutionary microbiology*, 50 Pt 1:347–353, January 2000. ISSN 1466-5026. doi:10.1099/00207713-50-1-347.